II. REMARKS

Claim Amendments:

Rejection Under 35 U.S.C. § 102 over Skov et al.

Claims 1, 3-7, 14-16 and 18-20 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Skov. More particularly, the Examiner has indicated that the reference teaches alkyl-substituted imidazoles.

Applicants respectfully request reconsideration of the following explanation of the Skov reference which appeared on page 8 of the response filed April 29, 2002.

> "Skov (Skov et al., U.S. Patent 4,921,963) teaches square planar complexes of platinum II, containing one radiosensitizing ligand and one "amine or ammine" ligand. Those radiosensitizing ligands are selected from a mononitro-substituted pyrazole, a mononitro-substituted imidazole, a mononitro-substituted thiazole and a mononitro-substituted isothiazole (col.3, lines 37-40). As was previously stated, claim 1 as amended recites only alkyl substituents for the heterocyclic moieties listed in claim 1. Accordingly, Skov no longer anticipates the instant invention."

As discussed, the compounds disclosed in Skov all contain nitro substitutions. In contrast, claim 1 includes the following limitation: "wherein all substituents on the heterocycle are alkyl substituents" (emphasis added). This limitation excludes the nitro-substituted compounds disclosed by Skov.

Rejection Under 35 U.S.C. § 103 over Skov

Claims 1, 3-7 and 14-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Skov. More particularly, the Examiner has indicated that Skov teaches alkyl substitutions. Applicants respectfully request reconsideration of the following explanation of the Skov reference which appeared on page 9 of the response filed April 29, 2002.

> "Applicants believe that Skov teaches away from the compounds claimed in the instant invention. Skov teaches that "the nitro group is a prerequisite for

activity, as it supplies the electron affinity to the ligand" (col. 5, lines 8-10). As such, there is no motivation or suggestion made by Skov to use other substituents, such as Applicants' claimed alkyl substituents instead of mononitro- substituents. Thus, Skov cannot render Applicants' claimed invention obvious. For these reasons, Applicants respectfully request reconsideration of this ground for rejection."

As discussed, Skov clearly teaches away from alkyl substitutions as the only substitution, since Skov emphasizes the importance of nitro substituents.

In addition, the Examiner made the following statement regarding the claims on page 3 of the Office Action:

"In addition, applicants' amended claims state that the heterocycle amine has at least one alkyl substituent, which could be interpreted to mean that there could be other substituents such as a nitro group as long as there is an alkyl group substition".

Applicants respectfully disagree with this interpretation. As stated previously, claim 1 recites the following limitation: "wherein all substituents on the heterocycle are alkyl substituents". This unambiguously excludes compounds with nitro group substitutions.

Rejection Under 35 U.S.C. § 103 over Murrer

Claims 1, 3-7 and 14-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Murrer. More particularly, the Examiner has indicated that Murrer teaches the equivalence of pyridine and other 5- or 6-membered heterocyclic amines at column 1, lines 39-42, and that Murrer also teaches alkyl substitutions. Applicants respectfully request reconsideration of the following explanation of the Skov reference which appeared on pages 9-10 of the response filed April 29, 2002.

"As amended herein, the claims now recite a select group of compounds having one of four types of heterocyclic amine moieties with alkly substituents. Murrer, in contrast, teaches hundreds of thousands of different compounds having any type of substituted amine moiety.

In *In re Baird* (29 USPQ 2d 1550 (1994)), a generic diphenol formula was held not to render obvious a particular bisphenol compound, because "there is nothing in the disclosure of Knapp suggesting that one should select such variables. Indeed, Knapp appears to teach away from the selection of bisphenol A by focusing on more complex diphenols..." (*Id.*, at 1552.) Likewise, in the instant case, Murrer teaches a plethora of different substituted amines, and makes

no suggestion to select Applicants' four claimed heterocyclic amines with alkyl substitutions. Moreover, Murrer's focus on pyridine with a single ring nitrogen teaches away from Applicants' claimed compounds each having two ring nitrogens. For these reasons, Applicants believe that Murrer does not render the claims as amended herein obvious, and respectfully request reconsideration of this ground for rejection."

Applicants would like to point out to the Examiner that the Murrer patent, which is also owned by Applicant, was discuss in the specification on page 3 as follows:

"U.S. patent 5,665,771 describes and claims a genus which contains the compounds of the present invention. The invention compounds, however, are not specifically taught or suggested in the above-referenced patent, and have improved solubility and/or antitumor activity characteristics as compared to the compounds exemplified in the '771 patent"

In the Office Action, the Examiner seems to be taking the position that, since Murrer teaches that the substituted amine can be a heterocyclic group and that the substituent can be alkyl, "one ordinary skilled in the art would be motivated to modify the compounds to arrive at the instant invention" (Office Action, page 3.) If this were the case, then Murrer would render obvious any substituted amine with any subtituent. This is simply inconsistent with well-settled legal principles regarding when a genus renders a species obvious.

III. SUMMARY

For the foregoing reasons, Applicants believe the amendments presented herein place the claims in condition for allowance. Reconsideration of the amended claims is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**".

Also attached is an Exhibit A which presents information about esters.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **39144-20043.00**.

Respectfully submitted,

Dated: September 5, 2002

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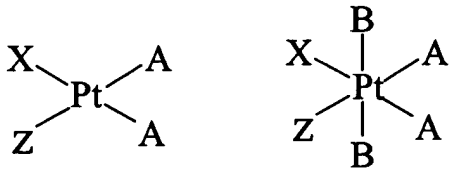
VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the above-captioned application as follows:

In the Claims:

Please amend the claims as follows:

1. (Twice amended) A *cis*-platinum complex of the formula Ia or Ib



Ia Ib

or a pharmaceutically acceptable salt thereof

wherein:

each A is independently [an anion] halo, hydroxy or carboxylate;

each B is independently halo, hydroxy, carboxylate, carbamate ester or [a] carbonate ester;

Z is a substituted 5- or 6-membered heterocyclic [moiety] amine selected from the group consisting of pyrazole, imidazole, oxazole and pyrazine, said heterocyclic amine having at least one alkyl substituent, wherein [at least one] said alkyl substituent sterically hinders access of the Pt atom to a DNA strand of a tumor cell [by a measurable amount more than an unsubstituted heterocyclic moiety with the same structure when tested under the same conditions, and wherein Z is other than pyridine], and wherein all substituents on the heterocycle are alkyl substituents; and

X is NH_3 or mono- or dialkyl substituted NH_3.

14. (Amended) The complex of claim [12] 1 wherein Z is 1,3,5-trimethylpyrazole.

15. (Amended) The complex of claim 1 wherein said [at least one] alkyl substituent is coupled to the heterocycle at a position [other than the position adjacent to] one atom removed from the coordinating atom in said heterocycle.